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(54) Title: REDUCED ALCOHOL MOUTHWASH ANTISEPTIC AND ANTISEPTIC PREPARATIONS

(57) Abstract

Reduced alcohol antiseptic mouthwash compositions are achieved which have the same oral antimicrobial efficacy, clarity and taste as higher alcohol level compositions. Availability of the active ingredients is best maintained by increasing the levels of surfactant employed in the composition together with the addition of two co-solvents, propylene glycol and glycerin. Propylene glycol with artificial sweetener(s), or propylene glycol alone with corresponding increases in the levels of surfactant are only marginally acceptable.

REDUCED ALCOHOL MOUTHWASH ANTISEPTIC AND ANTISEPTIC PREPARATIONS

FIELD OF THE INVENTION

This invention is directed to reduced alcohol antiseptic and mouthwash compositions in which the clarity, taste and efficacy of the antiseptic mouth rinse is comparable to higher alcohol level formulations.

BACKGROUND OF THE INVENTION

Thymol is a well known compound which is utilized for its antimicrobial activity in a variety of preparations. In particular, thymol can be utilized in oral hygiene preparations such as mouth rinses in sufficient quantities to provide desired beneficial therapeutic effects. Listerine® is a well known antiseptic mouth rinse that has been used by millions for over one hundred years and has been proven effective in killing bacteria in the oral cavity that are responsible for plaque, gingivitis and bad breath. Thymol, methyl salicylate, menthol and eucalyptol are active ingredients in antiseptic mouth rinses such as Listerine® and achieve their efficacy although present in very minute amounts. Without being restricted to any specific theory, it is now believed that efficacy and taste of antiseptic mouth rinses such as Listerine® is due to the availability or

together with thymol, menthol and eucalyptol. Methyl salicylate is not present and therefore not all four of the active ingredients are present.

It is therefore an object of the present invention to provide an antiseptic mouthwash formulation that is both efficacious in terms of killing the organisms responsible for plaque, periodontal disease and bad breath while at the same time providing such efficacy using reduced levels of alcohol and maintaining the characteristic organoleptic properties of Listerine® and other similar antiseptic-type mouth rinses. The efficacy, taste retention and clarity attributes are achieved at reduced alcohol levels of approximately 21.0% v/v by employing the surfactant levels from above 0.10% to less than 0.6% w/v. While it was believed that the non-ionic surfactant entraps a portion of the active ingredients and as such the suppressed dissolution/availability of actives would result in a reduction of efficacy as well as diminish the strong phenolic bite of the mouthwash, it was surprisingly and unexpectedly found that the addition of two co-solvents, propylene glycol and glycerin, in amounts whose combined percentage is less than the percent decrease in alcohol, enable the production of a reduced alcohol antiseptic mouthwash composition with levels of antiseptic efficacy and clarity, and desired organoleptic properties comparable to those of Listerine®.

0.03 to about 0.09% by weight and most preferably from about 0.04 to about 0.07%, said % by weight being based on the total composition. In addition to these actives, benzoic acid is preferably present in amounts of about 0.1 to about 0.3% by weight, based on the total composition and most preferably from about 0.13 to about 0.18%.

Compositions or final products containing these active ingredients include liquid oral preparations such as a mouthwash spray or rinse. In such preparations, the vehicle, i.e. the carrier for the ingredients of the mouthwash, such as the actives, and the like, is typically a water-alcohol mixture. Generally the ratio of water to alcohol is in the range of from about 3:1 to about 25:1, preferably about 3.2:1 to about 20:1 and most preferably, about 3.5:1 to about 10:1 by volume. The total amount of water-alcohol mixture in a mouthwash preparation is typically in the range from about 80% to about 99.9% by volume of the total composition.

The co-solvents which are added to effectively aid in the dissolution of the active ingredients can be present in amounts to about 9.0% v/v each, the total amount of the co-solvents not to exceed about 16% v/v. Preferably, the propylene glycol will be present in an amount of from about 1.0 to about 4.0% v/v while the glycerin will be in an amount of from about 0.2 to about 3.0% v/v or will exist in ratios of from about 20:1 to about 1:3, propylene glycol/glycerin, respectively.

salt of the monosulfated monoglycerides of hydrogenated coconut oil fatty acids; higher alkyl sulfates, such as sodium lauryl sulfate; sodium alkylether sulfates such as sodium laurylether (1-4) sulfate, alkyl aryl sulfonates, such as sodium dodecyl benzene sulfonate; higher alkyl sulfoacetates; alkyl and alkylether phosphates such as sodium laurylether (4) phosphate; higher fatty acid esters of 1,2-dihydroxy propane sulfonates; ether sulfates; alkyl phosphates; and substantially saturated higher aliphatic acyl amides of lower aliphatic amino carboxylic acids such as those having 12 to 16 carbons at the fatty acid; alkyl or acyl radicals. Examples of the last mentioned amides are N-lauroyl sarcosine, and the sodium, potassium, and ethanolamine salts of N-lauroyl, N-myristoyl or N-palmitoyl sarcosine.

The non-ionic surfactants employed are poly(oxyethylene)-poly(oxypropylene) block copolymers. Such copolymers are known commercially as poloxamers and are produced in a wide range of structures and molecular weights with varying contents of ethylene oxide and propylene oxide. The non-ionic poloxamers according to the invention are non-toxic and acceptable as direct food additives. They are stable and readily dispersible in aqueous systems and are compatible with a wide variety of formulating ingredients for oral preparations. These surfactants should have an HLB (Hydrophilic-Lipophilic Balance) of between about 10 and 30 and preferably between 10 and 25.

as the above described poly(oxyethylene)-poly(oxypropylene) block copolymers.

Other non-ionic surface active agents which may be suitable include condensates of sorbitan esters of fatty acids with from 20 to 60 moles of ethylene oxide (e.g., "Tweens"® a trademark of ICI United States, Inc.). Amphoteric agents such as quaternized imidazole derivatives and mixtures thereof may also be suitable.

Additional non-ionic surfactants which may be suitable are the condensation products of an alpha-olefin oxide containing 10 to 20 carbon atoms, a polyhydric alcohol containing 2 to 10 carbons and 2 to 6 hydroxyl groups and either ethylene oxide or a mixture of ethylene oxide and propylene oxide. The resultant surfactants are polymers having a molecular weight in the range of 400 to about 1600 and containing 40% to 80% by weight of ethylene oxide, with an alpha-olefin oxide to polyhydric alcohol mole ratio in the range of about 1:1 to 1:3.

Cationic surface active agents which may be suitable are molecules that carry a positive charge such as cetylpyridinium chloride.

Fluoride providing compounds may be present in the oral preparations of this invention. These compounds may be slightly water soluble or may be fully water soluble and are characterized by their ability to release fluoride ions or fluoride containing ions in water. Typical fluoride providing

added in ratios of from about 20:1 to about 1:3, respectively and to this resulting mixture a sufficient quantity of water is added to make up one liter.

Those skilled in the art will appreciate that the total amount of all ingredients (components) used in the compositions of this invention equals 100% by weight of the total composition. Also, unless stated otherwise, all percents herein are percent by weight of the total composition.

The following examples are illustrative only and should not be construed as limiting the invention in any way. Those skilled in the art will appreciate that variations are possible which are within the spirit and scope of the appended claims.

FORMULATION C

Ingredient	Ingred. Quantity Per Liter of Final Solutions
1) Alcohol USP (95% Ethanol)	227.3700 mls
2) Eucalyptol	.9220 gms
3) Thymol NF	.6390 gms
4) Menthol USP	.4250 gms
5) Acid Benzoic USP	1.5000 gms
6) Hydrochloric Acid (10% V/V)	
7) Sodium Hydroxide. 10% W/V Solution	
8) Methyl Salicylate NF	.6000 gms
9) Caramel. Acid Proof	.2150 gms
10) Poloxamer 407	1.4000 gms
11) Glycerin USP Special	5.0000 mls
12) Propylene Glycol USP	25.0000 mls
13) Water Potable	QS to 1.0000 L

FORMULATION D

Ingredient	Ingred. Quantity Per Liter of Final Solutions
1) Alcohol USP (95% Ethanol	227.3700 mls
2) Eucalyptol	.9220 gms
3) Thymol NF	.6390 gms
4) Menthol USP	.4250 gms
5) Acid Benzoic USP	1.5000 gms
6) Hydrochloric Acid (10% V/V)	
7) Sodium Hydroxide. 10% W/V Solution	
8) Methyl Salicylate NF	.6000 gms
9) Caramel. Acid Proof	.2150 gms
10) Poloxamer 407	1.5000 gms
11) Propylene Glycol USP	50.0000 mls
12) Water Potable	QS to 1.0000 L

The alcohol, eucalyptol, thymol, menthol, benzoic acid, methyl salicylate, poloxamer, glycerin and propylene glycol are added together and mixed until complete dissolution is achieved. Water is then added in a sufficient quantity so that the volume is brought to 950 mls. Hydrochloric acid or sodium

water, varying volumes of propylene glycol and glycerin were added to the samples. The samples were then analyzed with the turbidimeter. Additionally, a sample was prepared according to the ·250 formula, Formulation C set forth in Example I, (with 0.14% w/v Pluronic) and analyzed similarly. The results are listed in the following table. All percentages in the table are v/v.

FORMULATION	TURBIDITY (N.T.U.)
0% propylene glycol, 0% glycerin	>200 (off scale)
0% propylene glycol, 2% glycerin	70
1% propylene glycol, 1% glycerin	20
2% propylene glycol, 0% glycerin	8.7
2% propylene glycol, 2% glycerin	5.9
2.5% propylene glycol, 0.5% glycerin	4.5
Formulation C	<0.1 (off scale)

These results indicate that the mixture of the two cosolvents reduced the level of turbidity to a greater extent than did either of the individual solvents.

Example III

In vitro efficacy assessments using the plaque penetration assay model have been correlated to clinical investigations. Both Listerine® and Listerine Cool Mint® have been shown to be clinically effective and both products were

What We Claim Is:

1) A reduced alcohol antiseptic mouthwash composition comprising an effective amount of thymol, eucalyptol, methyl salicylate and menthol dissolved in no more than 22% v/v alcohol, a surfactant, propylene glycol, glycerin, benzoic acid, and water.

2) The reduced alcohol antiseptic mouthwash composition of claim 1 wherein said surfactant is selected from the group consisting of anionic, non-ionic, amphoteric and cationic surface active agents.

3) The reduced alcohol antiseptic mouthwash compositions of claim 2 wherein said non-ionic surfactants are selected from the group consisting of poloxamers.

4) The reduced alcohol antiseptic mouthwash compositions of claim 3 wherein said poloxamer constitutes from 0.01 - 0.2 weight percent of the total mouthwash composition.

5) The reduced alcohol antiseptic mouthwash composition of claim 4 wherein said glycerin and propylene glycol are present in amounts up to 6.0% volume of the total mouthwash composition.

12) The reduced alcohol antiseptic mouthwash of claim 11 wherein said menthol is present in an amount of from about .03% to about 0.05% w/v.

13) The reduced alcohol antiseptic mouthwash of claim 12 wherein said methyl salicylate is present in amounts of from about .04% to about .07% w/v.

14) A reduced alcohol antiseptic mouthwash composition consisting of no more than 22.0% v/v alcohol that is efficacious in the killing of oral microorganisms as it retains its clarity and characteristic bitter taste.

15) A reduced alcohol antiseptic mouthwash composition comprising an effective amount of thymol, eucalyptol, methyl salicylate and menthol dissolved in no more than 22.0% v/v alcohol, and further comprising a surfactant, propylene glycol, benzoic acid and water.

16) A reduced alcohol antiseptic mouthwash composition comprising an effective amount of thymol, eucalyptol, menthol, methyl salicylate, propylene glycol, glycerin, benzoic acid, an artificial sweetener and water.

17) The reduced alcohol antiseptic mouthwash composition of claim 16 wherein said artificial sweetener is selected from

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 94/00379

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A61K7/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP,A,0 497 476 (COLGATE-PALMOLIVE) 5 August 1992 see claims 1,4-7,15,16; examples a,c ---	1-3,7-17
Y	EP,A,0 338 978 (WARNER-LAMBERT COMPANY) 25 October 1989 see claims 1-12; table 1 & US,A,4 945 087 (TALWAR ET AL.) cited in the application ---	1-3,7-17
Y	JANISTYN 'Handbuch der Kosmetika und Riechstoffe, band 3, Die Körperpflegemittel' 1973 , HüTHIG , DE see page788, example " Mundwasser amerikanische Type " --- -/--	1-3,7-17

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 March 1994	13. 04. 94

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Fischer, J.P.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
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